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| 10/549,886 | 09/13/2006 | Torsten Muller | B1180/20044 | 7569 |
| 3000 7590 08/17/2009 CAESAR, RIVISE, BERNSTEIN, COHEN & POKOTILOV, LTD. 11TH FLOOR, SEVEN PENN CENTER 1635 MARKET STREET PHILADELPHIA, PA 19103-2212 | | | | |
| EXAMINER KAUR, GURPREET | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

Office Action Summary

Application No.

10/549,886

Applicant(s)

MULLER ET AL.

Examiner

GURPREET KAUR

Art Unit

1795

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 21-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-33 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☒ Information Disclosure Statement(s) (PTO/SF/ICE)
Paper No(s)/Mail Date 11/01/2008
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-20, drawn to method for separating particles in a microfluidic system.

Group II, claim(s) 21-28, drawn to microfluidic system.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Both of the inventions recite the use of microfluidic system as indicated in claim 1. The subject matter was determined to lack inventive step in Benecke et al. (U.S. Pat. No. 5,454,472). Accordingly, the invention lacks a common special technical feature that makes a contribution over the art.

During a telephone conversation with David Tener on July 22, 2009 a provisional election was made without traverse to prosecute the invention of group I, claims 1-20. Affirmation of this election must be made by applicant in replying to this Office action. Claims 21-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result**

in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

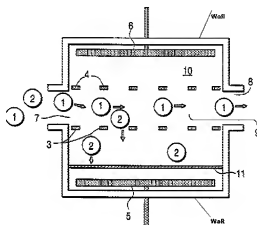
Claims 1-3, 7, 10-13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Benecke et al. (U.S. Pat. No. 5,454,472).

Regarding claim 1, Benecke et al. teaches a method for separating particles (1, 2) in a compartment (chamber 10) of a microfluidic system (see col. 1, lines 11-15) comprising the steps:

moving through the compartment a liquid in which particles (1 and 2) are suspended with a predetermined direction of flow (see col. 1, lines 11-15 and figure 1),
generating a deflection potential (electrophoretic effect) to move at least part of the particles (2) in the direction of deflection (see col. 5, lines 52-58 and figure 1),
one focusing potential (guiding field) to move at least part of the particles (1) opposite to the direction of deflection by dielectrophoresis under an effect of high-frequency electrical fields (see col. 5, lines 49-52, col. 3, lines 50-55 and see figure 1),

guiding particles with different dielectric properties into different flow areas (flow paths of particles 1 and 2) to separate particles (see col.1, lines 60-67 over to col. 2 and figure 2)

FIG. 1



Regarding claim 2, direction of deflection (path of particles 2) is orthogonal to the direction of the flow (path of particles 1) (see figure 1).

Regarding claim 3, the direction of the deflection (path of particles 2) is orthogonal to the direction of the flow towards one of the plurality of lateral walls of the chamber (10), the deflecting potential is generated by electrical force, and flow areas comprises flow paths (flow paths of particles 1 and 2) corresponding to different potential minima by applying focusing and deflection potentials during the passage through the channel under high-frequency alternating fields (see col. 1, lines 59-67 over to col. 2).

Regarding claim 7, Benecke et al. teaches that electrodes (22 and 28) are arranged along the walls of the channel (24) and electrodes (22) are loaded with electrical field for generating dielectrophoresis and electrodes (28) loaded with electrical field for generating electrophoresis (see col. 6, lines 1-18 and figure 2).

Regarding claims 10 and 11, Benecke et al. teaches an embodiment wherein plurality of focusing potentials are generated with electrode array (potentials generated by electrodes 22) between two electrodes (28) and the dielectric particles are guided onto separate flow paths (branch channels 27) (see figure 2)

Regarding claims 12 and 13, Benecke et al. teaches an embodiment wherein the two flow paths (flow paths of particles 1 and 2) empty into separated compartments (branch channels 27) separated by compartment wall (isolating layer 26) (see col. 6, lines 1-18 and figure 2).

Regarding claim 15, the particles (1 and 2) flow in front of the electrodes (3 and 4) during dielectrophoresis (see col. 3, lines 5-8 and figure 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 4, 6, 8, 9, 14, 16, 17, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benecke et al. (U.S. Pat. No. 5,454,472).

Regarding claim 4, Benecke et al. does not teach specifically a deflecting potential is formed by a direct voltage field.

However, Benecke et al. does teaches a homogenous field (electrophoretic force) is applied as the deflection force (see col. 2, lines 22-24). It is obvious to a person of ordinary skill in the art that a homogenous field can be a direct voltage and under applied field the particles are drawn to lateral walls of the compartment (see figure 1).

Regarding claim 6, Benecke et al. does not teach specifically separation of particles occurs under direct voltage field.

However, Benecke et al. does teaches the method of separating mixture of microscopic particles such as biological cells and cell organelles under applied homogenous field (see col. 1, lines 1-20 and col. 2, lines 22-24), It is obvious to a person of ordinary skill in the art that a homogenous field can be a direct voltage.

Regarding claims 8 and 9, Benecke et al. does not teach specifically that the deflecting and focusing potentials are generated alternating in time.

However, Benecke et al. does indicate that the deflecting and focusing potentials are generated via high frequency alternating voltage along the channel (see col. 3, lines 48-67). Furthermore, Benecke et al. teaches a homogenous field (electrophoretic force) is applied as the deflection force (see col. 2, lines 22-24). Particle 2 is deflected out of the path by deflecting field and particle 1 moves along the flow (see figure 1), therefore it would be obvious to a person of ordinary skill in the art that both the deflecting and focusing potential are applied alternately to force the particles in different directions.

Regarding claim 14, Benecke et al. does not teach specifically that the direction of deflection force and focusing potentials are parallel to each other.

However, Benecke et al. teaches a homogenous field (electrophoretic force) is applied as the deflection force (see col. 2, lines 22-24 and figure 1), therefore the direction of deflection is parallel to direction of flow and several focusing potential (dielectrophoresis force generated by row of electrodes 3 and 4) are parallel with direction of deflection (see figure 1), therefore it would be obvious to person of ordinary skill in the art that both the fields are superposed which would lead particles to run at different speeds.

Regarding claims 16 and 17, Benecke et al. does not teach specifically a pH gradient is generated in the channel by DC field.

However, Benecke et al. teaches a homogenous field is applied as the deflection force (see col. 2, lines 22-24), it is obvious to person of ordinary skill in the art a homogenous field can be a direct voltage and therefore it would be obvious to person of ordinary skill in the art that under applied homogenous field a pH gradient is generated in the channel.

Regarding claim 19, Benecke et al. does not teach specifically deflecting and focusing potentials are formed by superposed voltages.

However, Benecke et al. does teach that the deflecting (electrophoretic effect) and focusing (dielectrophoresis) potential are applied at alternating voltages with different frequencies (see col. 3, lines 57-61 and col. 4, lines 1-9). It is obvious to person of ordinary skill in the art that both the applied potentials are superposed in a chamber to move the particles (1 and 2) in two different directions.

Regarding claim 20, Benecke et al. does not teach specifically deflecting potentials are generated with different directions.

However, Benecke et al. teaches two deflection paths (branch channels 27) wherein the traveling field conveys the separated particles into the channels (see col. 6, lines 19-24), therefore it is obvious to person of ordinary skill in the art that two

deflecting potentials in different directions were applied to cause the particles to move in separate channels.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Benecke et al. (U.S. Pat. No. 5,454,472) as applied to claims 1-3, 10-13 and 15 above, and as further evidenced by Culbertson et al. (U.S. Pat. No. 6,783,647).

Regarding claim 5, Benecke et al. does not teach biological cells which are part lysed under direct voltage field.

However, Benecke et al. teaches the method of separating mixture of microscopic particles such as biological cells and cell organelles under applied homogenous field (see col. 1, lines 1-20 and col. 2, lines 22-24), it is obvious to person of ordinary skill in the art that a homogenous field can be a direct voltage.

Moreover, it is well known in the art, lysis of cells occur under applied electric field as further evidenced by Culbertson et al. (see col. 2, lines 6-9) to examine content of cells and expedite screening of cellular responses to drugs (see col. 3, lines 54-61).

Therefore it would be obvious to lysate the cells under applied electric field to examine content of cells and expedite screening of cellular responses to drugs.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Benecke et al. (U.S. Pat. No. 5,454,472) as applied to claims 1-3, 10-13 and 15 above, and further in view of Frumin et al. (U.S. Pub. No. 2001/0023825).

Regarding claim 18, Benecke et al. does not teach detection of particles take place after the guiding of the particles onto different flow paths.

However, Frumin et al. teaches a method of moving isolating and identifying particles under combined dielectrophoretic and electrophoretic field (see paragraph 0275) wherein the detection system detects the separated particles in different flow paths (see paragraph 0274 and figures 52C and 52D) in order to detect and extract cells in their respective flow paths.

Therefore it would be obvious to person of ordinary skill in the art at the time of the invention to incorporate the step of detecting the separated particles of Frumin et al. with the method of Benecke et al. to detect and extract cells in their respective flow paths.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GURPREET KAUR whose telephone number is (571)270-7895. The examiner can normally be reached on Monday-Friday (Alternate Friday Off), 8:00-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alexa Neckel can be reached on (571)272-1263. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G. K./
Examiner, Art Unit 1795

/Brian J. Sines/
Supervisory Patent Examiner, Art Unit 1795